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Impact of Reductions in Emissions from Major Source Sectors on Fine Particulate Matter–Related Cardiovascular Mortality

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Background: Reductions in ambient concentrations of fine particulate matter ($PM_{2.5}$) have contributed to reductions in cardiovascular (CV) mortality.

Objectives: We examined changes in CV mortality attributed to reductions in emissions from mobile, point, areal, and nonroad sources through changes in concentrations of $PM_{2.5}$ and its major components [nitrates, sulfates, elemental carbon (EC), and organic carbon (OC)] in 2,132 U.S. counties between 1990 and 2010.

Methods: Using Community Multiscale Air Quality model estimated $PM_{2.5}$ total and component concentrations, we calculated population-weighted annual averages for each county. We estimated $PM_{2.5}$ total- and component-related CV mortality, adjusted for county-level population characteristics and baseline $PM_{2.5}$ concentrations. Using the index of Emission Mitigation Efficiency for primary emission-to-particle pathways, we expressed changes in particle-related mortality in terms of precursor emissions by each sector.

Results: $PM_{2.5}$ reductions represented 5.7% of the overall decline in CV mortality. Large point source emissions of sulfur dioxide accounted for 6.685 [95% confidence interval (CI): 5.703, 7.667] fewer sulfate-related CV deaths per 100,000 people. Mobile source emissions of primary EC and nitrous oxides accounted for 3.396 (95% CI: 2.772, 4.020) and 3.984 (95% CI: 2.472, 5.496) fewer CV deaths per 100,000 people respectively. Increased EC and OC emissions from areal sources increased carbon-related CV mortality by 0.788 (95% CI: −0.540, 2.116) and 0.245 (95% CI: −0.697, 1.187) CV deaths per 100,000 people.

Discussion: In a nationwide epidemiological study of emission sector contribution to $PM_{2.5}$–related mortality, we found that reductions in sulfur-dioxide emissions from large point sources and nitrates and EC emissions from mobile sources contributed the largest reduction in particle-related mortality rates respectively. https://doi.org/10.1289/EHP5692

Introduction

The Clean Air Act Amendments of 1990 led to the establishment of national, regional, and source-specific regulations that significantly decreased ambient concentrations of fine particulate matter ($PM_{2.5}$) in many parts of the country (U.S. EPA 2017). The United States Environmental Protection Agency (EPA) estimated that the health and economic value of prevented health outcomes ($2 trillion) far outweigh the costs incurred to reduce emissions ($65 billion) (U.S. EPA 2011). However, the costs incurred to reduce emissions were not evenly distributed across the major emission source categories (mobile, areal, nonroad, large point sources, and other point sources). Therefore, these air quality control measures warrant continued evaluation of the public health benefits and an assessment of the contribution of emission reductions from each source.

Health effects of $PM_{2.5}$ exposures have been well documented, with the strongest evidence related to cardiovascular (CV) morbidity and mortality. Epidemiological studies showed that increased exposures to air pollution have been associated with increased mortality and morbidity (Schwartz et al. 1996; Dockery et al. 1993; Pope et al. 2002; Krewski et al. 2005; Cohen et al. 2017), whereas short-term improvements (Breitner et al. 2009; Wang et al. 2009; Peel et al. 2010; Dockery et al. 2013; Su et al. 2015) and long-term reductions in concentrations (Pope et al. 2009; Correia et al. 2013; Gilliland et al. 2017; Russell et al. 2018; Corrigan et al. 2018; Henneman et al. 2019) have been associated with improved health outcomes. Variation in risk with respect to particle size and chemical composition as well as the source of $PM_{2.5}$ has also been reported in cohort-based studies showing the highest risk associated with elemental carbon (EC) and organic carbon (OC) on per unit mass and with sulfates on absolute scale (Ostro et al. 2015; Thurston et al. 2016; Lippmann 2014; Laden et al. 2000; Vedal et al. 2013). Combined with the evidence from animal, toxicological, and controlled human exposure studies, the body of scientific research supported a weight-of-evidence conclusion that a causal relationship exists between short- and long-term $PM_{2.5}$ exposures and cardiovascular health effects, including mortality (U.S. EPA 2009).

Since 1990, concurrent with reductions in ambient $PM_{2.5}$ concentrations, CV mortality decreased across the United States and other developed countries primarily due to improved health care and lifestyle. In the U.S. between 1980 and 2000, coronary heart disease mortality rates decreased by half, with 90% of the reduction attributable to better control of cholesterol and blood pressure, reduced prevalence of tobacco smoking, increased physical activity, and improvements in clinical treatments, but reductions were partially offset by increased rates of obesity and type-2 diabetes (Capewell et al. 2009). The combined effects ascribed by summing these major risk factors do not account for a meaningful portion of the decline (10%) in CV mortality, which remained the leading cause of death. Because $PM_{2.5}$ has been causally related to CV morbidity and mortality, we investigated the contribution of reductions in ambient $PM_{2.5}$ concentrations to the reduction in CV mortality and the relative contributions of the emission source sectors to the observed change.

This study examined which portion of the observed declining trend in CV mortality between 1990 and 2010 was associated with changes in ambient $PM_{2.5}$ total and component concentrations (nitrates, sulfates, and EC and OC). Using the index of Emission Mitigation Efficiency (EME) (Wang et al. 2017), estimated $PM_{2.5}$, total- and component-related CV mortality was expressed relative to the change in precursor emissions by each of the major emission

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source sectors. We focused on four well-defined pathways of precursor emissions leading to the formation of $PM_{2.5}$ (nitrogen oxides emissions to nitrate $PM_{2.5}$, sulfur dioxide emissions to sulfate $PM_{2.5}$, primary EC emissions to EC $PM_{2.5}$, and primary OC to OC $PM_{2.5}$) from five major emission source sectors (mobile, areal, nonroad, large point sources, and other point sources).

Materials and Methods

Data Sources

Mortality data. Individual-level mortality data for each year between 1990 and 2010 were obtained from the U.S. National Center for Health Statistics. We calculated crude CV and chronic obstructive pulmonary disease (COPD) mortality rates for each 5-y age group, county, and year and used the overall U.S. age distribution in 2000 to calculate age-standardized county-level rates (Anderson and Rosenberg 1998). Annual county-specific CV mortality was expressed in deaths per 100,000 people.

The variance in CV mortality was calculated for each county and each year using standard formulas, which assumed the population was known and the number of deaths was distributed as a Poisson random variable (Murphy et al. 2013). Inverses of the variances in the annual CV mortality, which were proportional to county population, were used to weight the outcomes in the regression analysis. Annual CV and COPD mortality rates for each county were age-standardized to the overall U.S. population age distribution in 2000 to control for temporal and spatial variation in age distribution (Anderson and Rosenberg 1998). For the analysis, we used mortality rates from 2,132 counties with a population of at least 20,000 people, out of 3,109 counties in the contiguous United States.

Air quality data. We estimated annual average $PM_{2.5}$-total and component concentrations (sulfates, nitrates, EC, and OC) between 1990 and 2010 on a 36×36-km grid using the Community Multiscale Air Quality (CMAQ; version 5.0.2) framework, an emissions-based model of chemical formation and transport of pollutants in the atmosphere (Gan et al. 2015). To simulate air quality over the entire period, we used internally consistent historical emissions data from Xing et al. (2013) with lateral boundary conditions derived from the hemispheric simulations (Xing et al. 2015). The state-level historical anthropogenic emissions of sulfur dioxide (SO_2), nitrogen oxides (NOx), carbon monoxide, nonmethane volatile organic compound, ammonia, and particulate matter (PM_{10} and $PM_{2.5}$) for 49 sectors were developed from a consistent series of spatially resolved emissions, as described in (Xing et al. 2013). This approach used emission factors, time–activity data (vehicle miles traveled, tons of fuel sold in a county, etc.), and emission controls from various long-term databases, including the State Energy Data System. When compared with emissions calculated based on periodic emissions inventories, such as the National Emissions Inventory, this approach yielded a continuous and consistent inventory with smoother emission trends. In addition, emission trends for grid cells in the vicinity of monitoring stations showed good agreement with trends in ambient observed SO_2, NO_2, CO, and EC concentrations (Xing et al. 2013).

We used thin-plate smoothing, using the R software package "fields" (version 9.9; R Development Core Team) (Nychka et al. 2018), to interpolate $PM_{2.5}$ concentrations to population centroids of U.S. census tracts. We then calculated population-weighted averages across census-tract centroids to obtain annual $PM_{2.5}$ concentrations for each county and year.

Covariate data. The covariate set included time-variant and time-invariant factors that have been reported as explanatory or confounder variables for mortality and air pollution trends (Correia et al. 2013; Corrigan et al. 2018; Pope et al. 2009). Time-invariant factors were based on 1990 as a baseline year and included baseline year $PM_{2.5}$ concentrations and CV mortality for each county, median household income (base-10 log), percent of nonwhite population, and population (Bureau of Economic Analysis n.d.). For time-variant factors, the covariate set included age-standardized annual COPD mortality rates to account for the cumulative burden of smoking and annual smoking rates (Pope et al. 2009).

Analytic Approach

$PM_{2.5}$–related CV mortality trend. Our first analysis aimed to determine the portion of the temporal change in CV mortality attributable to the temporal change in the ambient concentration of $PM_{2.5}$. To achieve this objective, we fitted the following linear regression models:

$$Y_{st} = \mu_{1s} + \tau T_t + \theta_1 C_{st} + e_{1st}, \quad (1)$$

$$X_{st} = \mu_{2s} + \alpha T_t + \theta_2 C_{st} + e_{2st}, \quad (2)$$

$$Y_{st} = \mu_{3s} + \tau' T_t + \beta X_{st} + \theta_3 C_{st} + e_{3st}, \quad (3)$$

where for a single county s and year t, Y_{st} represented CV mortality, X_{st} represented $PM_{2.5}$ concentrations, and C_{st} represented time-variant and time-invariant covariate adjustment set variables. The temporal variable ($T_t = 1990 - Year_t$) represented years since the baseline year (1990), such that positive coefficients of temporal trends implied declines in $PM_{2.5}$ concentrations and CV mortality. Directed acyclic graph for this model is given in the Supplemental Figure S1(A).

The parameter set of interest (τ, α, β, τ') was estimated using the data from all counties and all years. First, we estimated the overall national temporal trend (τ) in annual CV mortality, measured in CV deaths per 100,000 persons per year, which accounted for the temporal changes in CV mortality adjusted for time-variant and time invariant covariates but not adjusted for $PM_{2.5}$ (Equation 1). Second, we estimated the national temporal trend (α) in annual $PM_{2.5}$ concentrations, measured in mass concentration ($\mu g/m^3$) per year, while adjusting for the covariates (Equation 2). Third, we estimated the association between $PM_{2.5}$ concentrations and CV mortality (β), measured in CV deaths (per 100,000 persons) per unit change in mass concentration ($\mu g/m^3$), assuming that this association was consistent nationally after adjusting for the covariates set C_{st} and for other time-varying changes in CV mortality unrelated to $PM_{2.5}$ concentrations (τ') (Equation 3). Finally, we calculated $PM_{2.5}$-related CV mortality as a product of the risk to CV mortality for each $\mu g/m^3$ change in $PM_{2.5}$ and the annual change in $PM_{2.5}$ concentrations ($\alpha\beta$).

Each model included a county-level random intercept to account for variation due to repeated measures from the same county and differences in baseline CV rates. Random errors in Equations 1–3 were assumed to have zero mean, and their variances were weighted by the inverse squared standard errors (SEs) of the CV mortality rate estimates at the baseline year 1990. Because the inverse squared SEs were proportional to the county population size, the weighted regressions accounted for spatial differences in the precision of the CV mortality estimates due to population. The same county-specific weights (W_s) scaled the random measurement error (σ_k^2) in all regressions to maintain consistent adjustment, such that the variance of random errors in regression k was $\mathrm{Var}(e_{k\,st}) = \sigma_k^2 W_s$.

To determine the portion of the temporal change in CV mortality accounted for by the temporal change in $PM_{2.5}$, we parsed the overall temporal trend in CV mortality (τ) into the non-$PM_{2.5}$–related trend (τ') and the $PM_{2.5}$-related trend ($\alpha\beta$). Generally, the temporal trend can be shown to exactly equal the

sum of the $PM_{2.5}$-related trend and non-$PM_{2.5}$–related trend in unadjusted models (MacKinnon et al. 2007; Hayes 2015). The SE of the $PM_{2.5}$-related CV mortality was estimated by the first-order approximation of the variance of the product:

$$SE(\widehat{\alpha\beta}) = \sqrt{(\widehat{\alpha}^2 + \sigma_\alpha^2)(\widehat{\beta}^2 + \sigma_\beta^2) - (\widehat{\alpha}\widehat{\beta})^2}, \quad (4)$$

where σ_α and σ_β are the SEs for the respective effects (Sobel 1982).

$PM_{2.5}$ Component–Related CV Mortality Trend

Our next analysis was to determine the proportion of the temporal change in CV mortality attributable to the temporal change in the ambient concentration of major $PM_{2.5}$ components. Annual concentrations of individual $PM_{2.5}$ components within county (nitrates, sulfates, EC, or OC) were highly correlated to each other and to the total $PM_{2.5}$ concentration during the time period considered (Supplemental Table S1). Therefore, the estimation of component-related CV mortality was adjusted for trends in total $PM_{2.5}$ concentration not associated with variation in that component over time through orthogonalization (Hastie et al. 2001; Schwartz et al. 2015). To control for the contribution of these $PM_{2.5}$ copollutants, we modified the single factor analysis by decomposing the total $PM_{2.5}$ concentrations (X_{st}) into the part explained by variation in a component (Z_{st}) and the part independent of the variation in the component (R_{st}) [Supplemental Figure S1(B)]. The independent portion was obtained using the residuals $R_{st} = (X_{st} - \widehat{X}_{st})$ from the regression of the total $PM_{2.5}$ concentration against the component concentration across all counties and years:

$$X_{st} = \mu_{0s} + \phi Z_{st} + \theta_0 C_{st} + e_{0st}. \quad (5)$$

The coefficient ϕ measured the estimated change in total $PM_{2.5}$ mass concentration per unit mass change in the component, adjusted for the covariates. The residuals represented the remaining portions of the total $PM_{2.5}$ concentration that could not be related to the component or the covariates. Statistically, the component Z_{st} and the residual R_{st} would not be correlated (because residuals did not vary within the linear space of the predictors), so the component and noncomponent estimated effects of $PM_{2.5}$ on CV mortality could then be jointly estimated without collinearity. We then fitted the following regression equations:

$$Z_{st} = \mu_{1s} + \alpha' T_t + \theta_1 C_{st} + e_{1st}, \quad (6)$$

$$R_{st} = \mu_{2s} + \alpha'' T_t + \theta_2 C_{st} + e_{2st}, \quad (7)$$

$$Y_{st} = \mu_{3s} + \tau'' T_t + \beta' Z_{st} + \beta'' R_{st} + \theta_3 C_{st} + e_{3st}, \quad (8)$$

where errors were again weighted by the inverse SEs for the 1990 CV mortality estimates. As in the single-factor analysis, α' and α'' measured temporal trends in $PM_{2.5}$-component concentrations and noncomponent concentrations (Equations 6 and 7), and β' and β'' measured the component and noncomponent CV mortality risk, adjusted for the covariates and the copollutants (Equation 8). The product $\alpha'\beta'$ then expressed the temporal trend in CV mortality attributed to a specific component Z_{st}, adjusted for the covariates C_{st} and for the changes in $PM_{2.5}$ mass concentration, which were unrelated variations in the component. An alternative to this approach could have adjusted for all components at once, but due to the high correlation between $PM_{2.5}$ components, the effect of each component individually could not be isolated from the effect of the mixture of components. Analysis for each $PM_{2.5}$ component was then conducted separately, repeating the same method to obtain the change over time trend (α'), the component-specific risk (β'), and the component-mediated portion of the CV mortality trend ($\alpha'\beta'$).

EME

In the final step of the analysis, we linked changes in total and component-specific $PM_{2.5}$–related CV mortality to a policy-relevant metric of changes in precursor emissions and their source sectors. Contribution of emissions from each source to the reduction in CV mortality was expressed in deaths per 100,000 persons accounting for the total change in concentrations, thus enabling direct comparison of contribution in absolute terms. We focused on four well-defined pathways of precursor emissions to $PM_{2.5}$ formations: nitrogen oxides (NOx) emissions to nitrate $PM_{2.5}$, SO_2 emissions to sulfate $PM_{2.5}$, primary EC emissions to EC $PM_{2.5}$, and primary OC to OC $PM_{2.5}$.

We used an EME index to relate changes in the precursor emissions to changes in particle-related CV mortality (Fann et al. 2009, 2012; Wang et al. 2017). We used the component-specific mortality risk coefficient from Equation 8 to connect total source emissions to component-related CV mortality at the national level. Emissions mitigated mortality expressed the change in component-related mortality in terms of the change in total mass of its precursor emissions.

To calculate EME for each of the four emission-to-$PM_{2.5}$ component pathways, we first calculated expected component-related mortality for each county as the product of the component-specific mortality risk coefficient (Equation 8) and the annual $PM_{2.5}$-component concentration ($U_{st}^z = \beta' \times Z_{st}$). We then averaged the component-related mortality over counties into the national average component-related mortality ($\bar{U}_t^z$) and regressed it against the total annual mass (V_t) of the precursor emission:

$$\bar{U}_t^z = \mu_4 + \lambda^z V_t + e_{4t}. \quad (9)$$

The estimated coefficent λ^z measured the EME for each of the four emission-to-$PM_{2.5}$ component pathways indexed by z, as the predicted change in national component-related CV deaths (per 100,000 persons) for every metric kiloton change in national precursor emissions. The positive EME indicated that reductions in emissions mitigated (reduced) component-related mortality.

The emission particle-specific EME was multiplied with the average change in emissions over the 20-y period to calculate total mitigated CV mortality in deaths per 100,000 persons. The average change in emission was also calculated for each of the five representative emission sources: mobile, nonroad, area, large point, and other point sources (Xing et al. 2013). Mitigated CV mortality by source-specific changes in emissions was then calculated based on changes in emissions from each source sector. Mobile sources included emissions from on-road gasoline and diesel vehicles. Nonroad sources incorporated emissions from other types of vehicles, such as construction equipment, trains, aircraft, and ships. The point sources included large sources, such as power plants and industrial facilities, and other smaller operations emitting combustion products. Areal sources included all other emission sources and a wide variety of emission products, such as wildland fires and open burning. Collectively, these sources accounted for anthropogenic primary emissions that preceded the development of the secondary $PM_{2.5}$ components. Definitions of each emission source category and relative contribution for each pollutant to each source can be found in Xing et al. (2013).

Table 1. Total $PM_{2.5}$- and component-related cardiovascular (CV) mortality trends: 2,132 U.S. counties, 1990–2010. The 20-y change was calculated by multiplying $PM_{2.5}$-related CV mortality trends by 20 y. The percent of the overall CV mortality trend was calculated as the ratio between the total CV mortality trend unadjusted for $PM_{2.5}$ (τ) and the $PM_{2.5}$-related CV trend ($\alpha\beta$).

	Total $PM_{2.5}$	Nitrates	Sulfates	Elemental carbon	Organic carbon
Weighted annual trend in $PM_{2.5}$ mass concentration (α: $\mu g/m^3$, per year)	0.134 (0.001) [0.132, 0.136]	0.0068 (0.0001) [0.0066, 0.0070]	0.0501 (0.0002) [0.0497, 0.0505]	0.00613 (0.00003) [0.00607, 0.00619]	0.0091 (0.0001) [0.0089, 0.0093]
Associated risk between $PM_{2.5}$ and CV mortality (β: deaths per 100,000 persons, per $\mu g/m^3$)	3.884 (0.161) [3.562, 4.206]	56.31 (1.49) [53.33, 59.29]	11.16 (0.44) [10.28, 12.04]	65.02 (2.69) [59.64, 70.40]	12.23 (0.87) [10.49, 13.97]
$PM_{2.5}$-related CV mortality trend ($\alpha\beta$: deaths per 100,000 persons, per year)	0.521 (0.022) [0.477, 0.565]	0.385 (0.011) [0.363, 0.407]	0.560 (0.022) [0.516, 0.604]	0.398 (0.017) [0.364, 0.432]	0.111 (0.008) [0.095, 0.127]
20-y change in $PM_{2.5}$ -related CV mortality [20 ($\alpha\beta$): deaths per 100,000 persons]	10.44 (0.44) [9.56, 11.32]	7.70 (0.22) [7.26, 8.14]	11.20 (0.44) [10.32, 12.08]	7.96 (0.34) [7.28, 8.64]	2.22 (0.16) [1.90, 2.54]
Percent of overall CV mortality trend [100 ($\alpha\beta$)/τ: percent]	5.7%	4.2%	6.1%	4.3%	1.2%

Note: When applicable, standard errors were reported in parentheses; 95% confidence intervals are reported in brackets.

Results

Overall Trends in CV Mortality and Air Quality

Ambient $PM_{2.5}$ concentrations decreased, on average, by 0.134 (95% CI: 0.133, 0.135) $\mu g/m^3$ each year (Equation 2; Table 1; Figure S2; Table S2). Concurrently, CV mortality rates (adjusted for baseline year mortality, baseline year $PM_{2.5}$, median household income, county-level percent nonwhite, and age-standardized COPD mortality) decreased on average by 9.196 (95% CI: 9.160, 9.232) deaths per 100,000 persons each year between 1990 and 2010 (Equation 1). Across the 2,132 counties studied, the Midwest and South had the highest baseline CV mortality rates in 1990, whereas annual reductions were highest throughout the Midwest and Northeast (Figure S3). Most areas observed an overall annual reduction in ambient concentrations, but areas with high baseline levels of $PM_{2.5}$ in 1990 experienced the largest annual reductions in concentrations (Figure S4). Among the main components of $PM_{2.5}$, sulfates changed by the largest amount, having decreased on average by 42.1% (95% CI: 41.9, 42.3) between 1990 and 2010 (Supplemental Table S2).

CV Mortality Rates Attributable to Trends in $PM_{2.5}$

The decrease in CV mortality rates can be apportioned to the declines in $PM_{2.5}$ concentrations. On average, each 1-$\mu g/m^3$ reduction in $PM_{2.5}$ was associated with 3.884 (95% CI: 3.562, 4.206) fewer deaths per 100,000 persons (Table 1; Table S3). When combined with the annual decline in $PM_{2.5}$ concentrations, the $PM_{2.5}$-trend accounted for 0.521 (95% CI: 0.477, 0.565) fewer deaths per 100,000 persons each year, for a total change of 10.44 (95% CI: 9.56, 11.32) fewer deaths per 100,000 persons over the whole period. As such, declines in $PM_{2.5}$ accounted for 5.7% of the total decline in CV mortality rates (Table 1).

As the average concentrations of $PM_{2.5}$ declined in most counties, $PM_{2.5}$-related CV mortality decreased across the continental United States (Figure 1). However, an increase in $PM_{2.5}$-related CV mortality trends was observed in counties commonly affected by wildland fires: the western United States and northern Florida.

CV Mortality Rates Attributable to Trends in $PM_{2.5}$ Components

When considering CV mortality reductions related to changes in $PM_{2.5}$-component concentrations, estimated risk varied across components in relative and absolute terms (Table 1; Table S4). Reductions in sulfates, elemental carbon and nitrates attributed the largest absolute reduction in CV mortality, with 11.20 (95% CI: 10.32, 12.08), 7.96 (95% CI: 7.28, 8.64) and 7.70 (95% CI: 7.26, 8.14) fewer CV deaths per 100,000 persons over the 20-y period, respectively (fourth row of Table 1). Therefore, reductions in sulfates had the largest attributable change in absolute terms. Reductions in EC and nitrates had the strongest association with changes in CV mortality per change in mass concentration, at 65.02 (95% CI: 59.64, 70.40) and 56.31 (95% CI: 53.33, 59.29) fewer deaths per 100,000 persons for each 1-$\mu g/m^3$ decrease in concentration of EC and nitrates, respectively.

Mitigation by Emission Source Sectors

The greatest total mitigation in $PM_{2.5}$-related CV mortality rates was attributed to the reductions in sulfate concentrations driven by the reductions in SO_2 (Table 2, second column). A 20-y reduction of 11.064 (95% CI: 9.834, 12.294) deaths per 100,000 persons was attributed to the mitigation of total SO_2 emissions. Reductions in SO_2 emissions from large point sources (such as power plants) represented the largest source sector for the decline sulfate-related CV mortality at 6.685 (95% CI: 5.703,7.667)

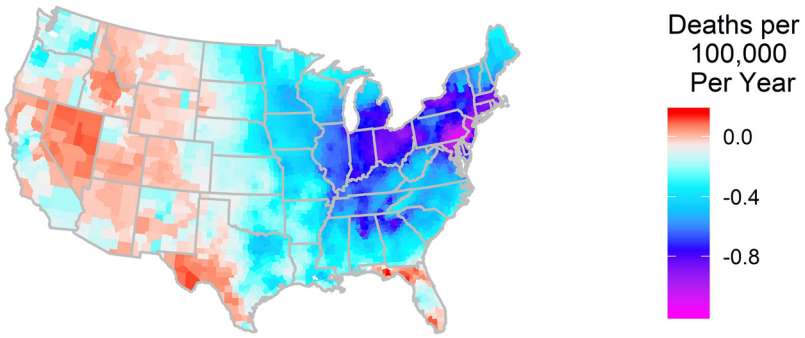

Figure 1. Map of $PM_{2.5}$-related reductions in cardiovascular mortality rates for contiguous U.S. counties, 1990–2010. $PM_{2.5}$-related reductions in age-standardized cardiovascular (CV) mortality rate were calculated as products of county-level annual trends in $PM_{2.5}$ and the nationally estimated association between $PM_{2.5}$ concentration and CV mortality.

deaths per 100,000 persons. Similarly, a reduction of 8.139 (95% CI: 4.957,11.321) deaths per 100,000 persons was attributed to the mitigation of NOx emissions with the largest contribution from mobile and large point sources.

EC-related CV mortality declined by 0.818 (95% CI: 0.684, 0.952) deaths per 100,000 persons per metric kiloton of reduced primary EC emissions, in comparison with 0.118 (95% CI: 0.082, 0.154), 0.022 (95% CI: 0.020, 0.024), and 0.022 (95% CI: 0.014, 0.030) fewer CV deaths per 100,000 persons for each metric kiloton of reduced OC, SO_2, NOx, respectively (Table 2). The estimated difference in CV mortality resulting from the absolute decline in EC emissions over the study period (3.637 fewer CV deaths per 100,000; 95% CI: 2.007, 5.267) represented 46% of the estimated decline in CV mortality rates related to reduced EC particle mass concentrations during the same time period (7.96 fewer CV deaths per 100,000; 95% CI: 7.28, 8.64) from Table 1. Reductions in EC emissions from the mobile sector accounted for the largest reductions in EC particle–related CV mortality over the study period (3.396 fewer CV deaths per 100,000; 95% CI: 2.772, 4.020), whereas a slight upward trend in EC emissions from the areal sector led to increased EC particle–related CV mortality (0.788 additional CV deaths per 100,000; 95% CI: −2.116, 0.540). In the CMAQ modeling framework, the areal sector included a variety of sources for EC emissions but was strongly influenced by emissions from wildfire events (Dennison et al. 2014).

Smaller reductions in OC particle–related CV mortality rates were attributed to primary OC emissions during the time (0.100 fewer CV deaths per 100,000; 95% CI: −0.850, 1.050) than reductions related to EC emissions. However, similar to the sources for EC emissions, reductions in OC emissions from the mobile sector accounted for the largest reductions in OC particle–related CV mortality (0.245 fewer deaths per 100,000; 95% CI: 0.167,0.323), whereas increased areal source emissions was attributed to 0.245 (95% CI: −1.187, 0.697) additional OC particle–related CV deaths per 100,000 people.

Discussion

In this research we characterized the portion of the CV mortality annual trend that can be explained by the changes in ambient concentrations of $PM_{2.5}$, its major chemical components, and their related emission source sectors, based on CMAQ modeling framework. We estimated that reductions in $PM_{2.5}$ accounted for 5.7% of the decline in CV mortality rates, or 10.44 (95% CI: 9.56, 11.32) fewer deaths per 100,000 persons between 1990 and 2010. We estimated that sulfates and elemental carbon played the most substantial role in reducing $PM_{2.5}$-related CV mortality. Sulfates had the greatest total impact, mainly due to substantial decreases in SO_2 emissions from power plants and similar sources. EC and nitrates had the greatest impact on health outcomes per unit of component mass, at 65.02 (95% CI: 59.64,70.40) and 56.31 (95% CI: 53.33, 59.29) fewer CV deaths per 100,000 persons per $\mu g/m^3$, respectively. These reductions were attributed mainly to reductions in mobile vehicle emissions, at 3.396 (95% CI: 2.772, 4.020) and 3.984 (95% CI: 2.472, 5.496) CV deaths per 100,000 persons, respectively. Changes in the OC contributed to reduction in CV mortality by mobile sources but increased the CV mortality burden due to increased emissions from areal sources, mostly driven by contribution of wildfires.

Previous studies using risk assessment methods have estimated public health benefits of environmental policies at the national level during the same period that we considered here. Risk assessments combined concentration–response functions from epidemiological studies with anticipated changes in ambient concentrations from a specific or hypothetical regulatory action to estimate the potential health benefit of interventions (Bell et al. 2011; Rich 2017; Fann et al. 2017; Lee et al. 2015; Boogaard and van Erp 2019; Brauer et al. 2016). Although these approaches provided useful projection of health impacts, they were subject to uncertainties related to concentration–response relationships of a different period, concentration range, and composition of ambient particles or population (Breitner et al. 2009; Dominici et al. 2007; Bell et al. 2011). In this study, we offer epidemiological analysis of the fraction of long-term trends in CV mortality that can be attributed to changes in total and component specific $PM_{2.5}$ based on the observed mortality trends. Using the index of EME, we expressed attributable change in CV mortality relative to the change in precursor emissions from each of the major emission-source sectors. Change in CV mortality was expressed as deaths per 100,000 persons, which enables comparison across emission sectors.

The estimated risk of CV mortality associated with change in total and component concentrations of $PM_{2.5}$ was consistent with estimated risks reported in cohort-based studies in which confounding by individual-level factors could be controlled (Ostro et al. 2015; Thurston et al. 2016). Ostro et al. (2015) examined the effects of chronic exposure to $PM_{2.5}$ on all-cause, CV, ischemic heart disease, and respiratory mortality in California using monitor-based exposures. Adjusted hazard ratios (HR) for ischemic heart disease mortality were 1.04 (95% CI: 0.94, 1.14) per 0.8-$\mu g/m^3$ increase in EC and 1.03 (95% CI: 0.91, 1.18) per 9.6-$\mu g/m^3$ increase in $PM_{2.5}$, corresponding to standardized HR of 1.05 and 1.003 for a 1-$\mu g/m^3$ increase in each exposure (or 5% and 0.3% increased mortality), respectively. HRs for mortality in association with sulfates, which were negligible in the California study area, were not reported.

Table 2. Emission mitigation efficiency (EME) and total mitigated cardiovascular (CV) mortality reductions by emission sources: 2,132 U.S. counties, 1990–2010. Total mitigated mortality equaled the product of the EME, the annual change in the emissions, and 20 y. CV mortality was measured in age-standardized CV deaths per 100,000 persons.

	EME	Total mitigated CV mortality between 1990 and 2010 (Deaths per 100,000 persons)					
Emission-PM relationship	(CV mortality, per metric kiloton)	Total emission	Areal	Non-road	Mobile	Large point	Other point
NOx to Nitrates	0.022 (0.004) [0.014, 0.030]	8.139 (1.591) [4.957, 11.321]	0.080 (0.098) [−0.116, 0.276]	0.436 (0.131) [0.174, 0.698]	3.984 (0.756) [2.472, 5.496]	3.055 (0.590) [1.875, 4.235]	0.585 (0.123) [0.339, 0.831]
SO_2 to Sulfates	0.022 (0.001) [0.020, 0.024]	11.064 (0.615) [9.834, 12.294]	0.904 (0.048) [0.808, 1.000]	0.059 (0.011) [0.037, 0.081]	0.354 (0.017) [0.320, 0.388]	6.685 (0.491) [5.703, 7.667]	3.061 (0.141) [2.779, 3.343]
Primary to $PM_{2.5}$ Elem. Carbon	0.818 (0.067) [0.684, 0.952]	3.637 (0.815) [2.007, 5.267]	−0.788 (0.664) [−2.116, 0.540]	0.637 (0.207) [0.223, 1.051]	3.396 (0.312) [2.772, 4.020]	0.121 (0.030) [0.061, 0.181]	0.271 (0.033) [0.205, 0.337]
Primary to $PM_{2.5}$ Organic Carbon	0.118 (0.018) [0.082, 0.154]	0.100 (0.475) [−0.850. 1.050]	−0.245 (0.471) [−1.187, 0.697]	0.008 (0.011) [−0.014, 0.030]	0.245 (0.039) [0.167, 0.323]	0.017 (0.004) [0.009, 0.025]	0.076 (0.012) [0.052, 0.100]

Note: Standard errors were reported in parentheses; 95% confidence intervals are shown in brackets.

Thurston et al. (2016) estimated associations between ischemic heart disease mortality and source-specific $PM_{2.5}$ components in 100 metropolitan areas across the United States. and reported adjusted HRs of 1.03 (95% CI: 1.00, 1.06) per 0.26-$\mu g/m^3$ increase in EC, 1.06 (95% CI: 1.02, 1.11) per 0.53-$\mu g/m^3$ increase in sulfur, and 1.03 (95% CI: 1.00, 1.06) per 3.13 $\mu g/m^3$ of $PM_{2.5}$, corresponding to standardized HRs of 1.12 (95% CI: 1.00, 1.25), 1.12 (95% CI: 1.04, 1.22), and 1.009 (95% CI: 1.00, 1.02) per 1-$\mu g/m^3$ increases in each exposure (12.0%, 11.6%, and 0.9% increases from baseline), respectively. Because a 0.53-$\mu g/m^3$ change in sulfur would correspond to 1.59 $\mu g/m^3$ of sulfates by molecular weight, the standardized HR for sulfates when converted was 1.037 (95% CI: 1.01, 1.07) per 1-$\mu g/m^3$ increase in sulfates, or 3.7% increase from baseline. Using age-standardized rates for all causes of CV mortality, we estimated that 1-$\mu g/m^3$ increases in EC, sulfates, and total $PM_{2.5}$ concentrations were associated with 65.02 (95% CI: 59.64, 70.40), 11.16 (95% CI: 10.28, 12.04), and 3.88 (95% CI: 3.56, 4.20) increases in CV deaths per 100,000 people, respectively, corresponding to 15.5%, 2.67%, and 0.9% increases relative to the average baseline mortality rate in 1990 [416.9 per 100,000 persons (95% CI: 415.9, 417.9); Table S1]. Although these risk estimates were remarkably consistent, the differences could be expected, due to variations in spatial and temporal distribution of underlying risk, outcome specific risk, or differences in methodological approaches.

For the air quality estimates, CMAQ model formulation provided spatially and temporally resolved estimates of total- and component-specific PM concentrations, which was particularly valuable for the assessment of trends in areas without air quality monitors. Air pollutant fields simulated by CMAQ were routinely used for air quality planning and forecasting and have previously been evaluated for their agreement with the observed data. Previous studies have shown that the trends in the total $PM_{2.5}$ and its components simulated by the coupled CMAQ model were highly correlated with observation data from monitors at the annual level and are similar both in direction and magnitude (Gan et al. 2016; Appel et al. 2017; Foley et al. 2010). The 1990–2010 CMAQ simulations used in this study represented the first effort in which decadal-scale CMAQ simulations were performed over the entire United States using a consistent set of model inputs and CMAQ configurations (model version and science options) for the entire time period. The 20-y CMAQ simulations used for this analysis allowed us to estimate trends in air quality and associations with CV mortality beginning in the early 1990s, before nationwide monitoring networks were fully established as a consequence of the 1990 Clean Air Act amendments.

The CMAQ model simulations used in this analysis could not be compared with observed data for the entire time period and spatial domain. However, the total and speciated $PM_{2.5}$ mass estimates have been compared with limited data from the Clean Air Status and Trends Network (CASTNET) and the Interagency Monitoring of Protected Visual Environments (IMPROVE) network for 1995–2010 (Gan et al. 2015). In addition, total and speciated $PM_{2.5}$ mass estimates from different versions of the CMAQ model have been extensively compared with observations from CASTNET, IMPROVE, and Chemical Speciation Network (CSN) for 2006 (Foley et al. 2010) and for 2011 (Appel et al. 2017). Those studies showed that model performance was generally best for sulfates, followed by other secondary inorganic aerosols (nitrate and ammonium) and EC, and lowest for OC. Consequently, associations between OC reductions and CV mortality trends observed in this study should be interpreted with caution.

The covariate adjustment set included time-variant and time-invariant factors that have been reported as explanatory or confounder variables for mortality trends in air pollution health studies (Correia et al. 2013; Corrigan et al. 2018; Pope et al. 2009). Time-invariant factors included baseline year $PM_{2.5}$ concentrations, baseline year CV mortality, median household income, and county-level percent nonwhite population. Time-invariant factors were used to account mainly for spatial variations in CV mortality unrelated to air quality. Time-varying factors included linear term for CV mortality annual trend and age-standardized COPD mortality rates, which have been used to account for the accumulated exposure to smoking in previous studies (Correia et al. 2013; Corrigan et al. 2018; Pope et al. 2009). Annual county-level CV mortality rates and COPD mortality rates were age-standardized to the U.S. population in 1990 to allow direct comparison of mortality rates between counties and across years, controlling for temporal and spatial variations in age distribution. Due to the high variance in estimated mortality rates for smaller populations, mortality data from counties with fewer than 20,000 people in 1990 were combined with the data from nearby counties or excluded entirely (Wang et al. 2013; Roth et al. 2017). The merging reduced the number of counties from 3,109 to 2,132, but selection bias was unlikely because the remaining counties were located throughout the continental United States.

Although we adjusted for several county-level characteristics identified as potential confounders in previous studies, we cannot exclude the possibility of residual confounding by other factors associated with CV mortality or $PM_{2.5}$ exposures, including other county-level factors (e.g., local economic disruptions) and individual-level factors (e.g., smoking or alcohol consumption). In addition, we did not evaluate factors that might modify the effects of county-level $PM_{2.5}$ and $PM_{2.5}$ components on CV mortality, such as differences in health care access or other socioeconomic disparities. Additionally, we explored only linear trends between annual CV mortality and $PM_{2.5}$ concentrations, but nonlinear trends could also be explored in future research. We used population-weighted average annual concentrations of $PM_{2.5}$ and components but did not consider variations within county or within year, and we cannot exclude the possibility of exposure misclassification. Finally, the scope of our health effects analysis was limited to overall CV mortality rates, but we measured neither the total burden of CV disease nor effects due to different subtypes of CV disease.

Our approach to estimating the effect of a single $PM_{2.5}$ component controlled for confounding by unrelated variation in the other components. Each component has its own risk estimate, carried though to a calculation of mitigated mortality. Mortality risk coefficients measured the extent that changes in CV mortality rates were associated to changes in the component concentration, but the toxicity would still be related to the entire mixture of particles that covariate with that component. Statistically, relative toxicity cannot be further differentiated based on observational data. Other analysis techniques for multiple correlated mediators might detect the combination of $PM_{2.5}$ components most strongly associated with trends in CV mortality but may not yield the effects attributable to individual components (VanderWeele and Vansteelandt 2014).

In summary, we presented a nationwide-trends analysis attributing a proportion of the long-term changes in CV mortality to long-term changes in total ambient $PM_{2.5}$ concentrations, specific $PM_{2.5}$ components, precursor emissions, and their source sectors. Linking changes in health burden to changes in precursor emissions by calculating component-specific CV mortality change, we express absolute change in risk to provide insights into the contribution of emission sectors to improved health outcomes. Further research would be needed to establish causal effects of specific regulations, but the overall improvement in air quality due to the combined reductions in SO_2, EC, and NOx emissions showed human health benefits. Because our analysis suggested SO_2 emissions and

emission from mobile sources as major drivers of reduced $PM_{2.5}$-related CV mortality rates, these regulatory programs may be the most pertinent for further accountability studies.

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A.G.R. conceived the study. G.C.P. carried out the data analysis. A.G.R. reviewed the mathematical framework. L.M.N. reviewed the epidemiologic model. R.M. and C.H. contributed the CMAQ model results. A.G.R, L.M.N., G.C.P., A.E.C. contributed to the discussion and interpretation of the results. All authors contributed to writing, review, and commenting on the paper.

Although this work has been reviewed for publication by the EPA, it does not necessarily reflect the views and policies of the agency.

All data needed to evaluate the conclusions in the paper are present herein or in the supplementary materials. Data used in this analysis will be posted on EPA Science Hub website with a unique DOI: 10.23719/1503961.

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